

# Towards A Self-Organized Agent-Based Simulation Model for Exploration of Human Synaptic Connections

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## Abstract

In this paper, the early design of our self-organized agent-based simulation model for exploration of synaptic connections that faithfully generates what is observed in natural situation is given. While we take inspiration from neuroscience, our intent is not to create a veridical model of processes in neurodevelopmental biology, nor to represent a real biological system. Instead, our goal is to design a simulation model that learns acting in the same way of human nervous system by using findings on human subjects using reflex methodologies in order to estimate unknown connections.

## 1. Introduction

The enormous complexity and the incredible precision of neuronal connectivity have fascinated researchers for a long time. Although considerable advances have been made during last decades in determining this cellular machinery, understanding how neuronal circuits are wired is still one of the holy grails of neuroscience. Neuroscientists still rely upon the knowledge that is obtained in animal studies. Thus, there remains a lack for human studies revealing functional connectivity at the network level. This lack might be bridged by novel computational modeling approaches that learn the dynamics of the networks over time. Such computational models can be used to put current findings together to obtain the global picture and to predict hypotheses to lead future experiments. In this sense, a self-organized agent-based simulation model for exploration of synaptic connectivity is designed that faithfully generates what is observed in natural situation. The

simulation model uses findings on human subjects using reflex methodologies to the computer simulations in order to estimate unknown connections.

Remaining of this paper is organized as follows. Section 2 gives background information, section 3 introduces our simulation model and section 4 summarizes the related work. Finally, section 5 gives the future work and concludes the paper.

## 2. Background

Roughly speaking, the central nervous system (CNS) is composed of excitable cells: neurons & muscles. A typical neuron can be divided into three functionally distinct parts, dendrites, soma and axon. The dendrites collect synaptic potentials from other neurons and transmits them to the soma. The soma performs an important non-linear processing step (called *integrate & fire model*): If the total synaptic potential exceeds a certain threshold (makes the neuron membrane potential to *depolarize* to the threshold), then a spike is generated [Gerstner and Kistler, 2002]. A spike is transmitted to another neurons via synapses. Most synapses occur between an axon terminal of one (presynaptic) neuron and a dendrite or the soma of a second (postsynaptic) neuron, or between an axon terminal and a second axon terminal (presynaptic modulation). When a spike transmitted by the presynaptic neuron reaches to a synapse, a post-synaptic potential (PSP) occurs on the postsynaptic neuron. This PSP can either excite or inhibit a postsynaptic neuron's ability to generate a spike.

To study functional connection of neurons in human subjects it has been customary to use stimulus-evoked changes in the discharge probability and rate of one or more *motor units* in response to stimulation of a set of periph-

eral afferents or cortico-spinal fibers. These are the most common ways to investigate the workings of peripheral and central pathways in human subjects. Although these are indirect methods of studying human nervous system, they are nevertheless extremely useful as there is no other method available yet to record synaptic properties directly in human subjects. Motor units are composed of one or more alpha-motoneurons and all of the corresponding muscle fibers they innervate. When motor units are activated, all of the muscle fibers they innervate contract. The output from the system is through the motoneurons, which is measured by reflex recordings from muscle. As output, the instantaneous discharge frequency values against the time of the stimulus and has recently been used to examine reflex effects on motoneurons, as well as the sign of the net common input that underlies the synchronous discharge of human motor units (for a review, see [Türker and Powers, 2005]). However, most of the synaptic input to motoneurons from peripheral neurons does not go directly to motoneurons, but rather to interneurons (whose synaptic connectivity is unknown) that synapse with the motoneurons.

### 3. An Agent-based Simulation Model for Human Motor Units

For exploring synaptic connectivity in human CNS, we designed and implemented a self-organized agent-based simulation model. Since it seems as a strong candidate for the simulation work and hence the solution to the problem of putting information together to predict hypotheses for future studies [Gürçan et al., 2010], we have chosen agent-based modeling and simulation (ABMS) technique. ABMS is a new approach to modeling systems and is composed of interacting, autonomous agents [Macal and North, 2006]. It is a powerful and flexible tool for understanding complex adaptive systems such as biological systems.

#### 3.1 Approach to Self-Organization

Our agent-based simulation model uses the AMAS theory [Capera et al., 2003] to provide agents with adaptive capabilities. This adaptiveness is based on cooperative behavior which, in this context, means that an agent does all it can to always help the most annoyed agent (including itself) in the system. When faced with several problems at the same time, an agent is able to compute a degree of criticality in order to express how much these problems are harmful for its own local goal. Considering this criticality, as well as those of the agents it interacts with, an agent is therefore able to decide what is the most cooperative action it has to undertake. The importance of the anomalies and how they are combined emerges from a cooperative self-adjusting process taking feedbacks into account.

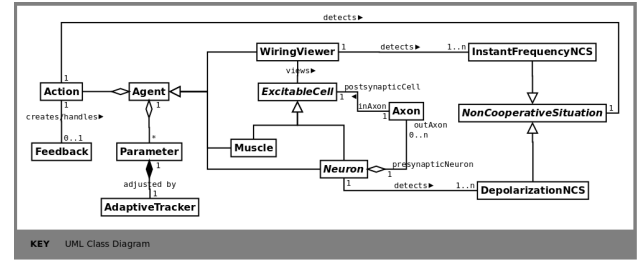


Figure 1. The simulation model for Self-Organizing Agents.

Bernon et al. [Bernon et al., 2009] proposed an approach resting on this theory for engineering self-modeling systems, in which same type of agents are all designed alike and all agents consist of four behavioral layers. An agent owns first a *nominal behavior* which represents its behavior when no situations that are harmful for its cooperative state are encountered. If a harmful situation occurs (such a situation is called a *non-cooperative situation*, or NCS) it has to be avoided or overcome by every cooperative agent. Therefore, when an agent detects a NCS, at any time during its lifecycle, it has to adopt a behavior that is able to process this NCS for coming back to a cooperative state. This provides an agent with learning capabilities and makes it constantly adapt to new situations that are judged harmful. The first behavior an agent tries to adopt to overcome a NCS is a *tuning behavior* in which it tries to adjust its internal parameters. If this tuning is impossible because a limit is reached or the agent knows that a worst situation will occur if it adjusts in a given way, it may propagate the NCS (or an interpretation of it) to other agents that will try to help it. If such a behavior of tuning fails, an agent adopts a *reorganisation behavior* in which it tries to change the way in which it interacts with others (e.g., by changing a link with another agent, by creating a new one, by changing the way in which it communicates with another one and so on). In the same way, for many reasons, this behavior may fail counteracting the NCS and the last kind of behavior may be adopted by the agent, the one of *evolution*. In this last step, an agent may create a new one (e.g., for helping it because it found nobody else) or may accept to disappear (e.g., it was totally useless). In these two last levels, propagation of a problem to other agents is always possible if a local processing is not achieved.

#### 3.2 The Simulation Model

Figure 1 shows the conceptual model of our simulation. *Neuron* and *Muscle* agents are treated as *ExcitableCells*. *Axons* are represented as connectors between neurons and excitable cells. Unitary behaviors that an agent is able to do are defined as *Actions*. These actions can be either for one shot or can be repeated with a specific interval. Each *Agent* is able to memorize, forget and spontaneously send feed-

backs related to non-desired configuration of inputs (by detecting NCSs). Each agent has various internal parameters (*Parameter*). When an agent receives feedbacks from one or more incoming entries, it is able to adjust its internal parameters or retro-propagates a *Feedback* to its own entries. For adjusting parameters of agents we used *Adaptive-Trackers*. Tuning a parameter for an agent consists in finding its right value within an interval considering that this value may evolve with time [Lemouzy et al., 2010]. Adaptive trackers allow this tuning depending on the feedbacks the agent gets from its environment.

In the AMAS approach, a system is said *functionally adequate* if it produces the function for which it was conceived, according to the viewpoint of an external observer who knows its finality. The external observer in our model is a *WiringViewer* agent. A *WiringViewer* agent is used to trigger the recruitment of synaptic connections and the functional connectivity of the neural system. It monitors and records the outputs of the neural system that take place over time to compare the simulated (running) data to reference data for detecting NCSs. Reference data could be either experimental data or a statistical mean of several experimental data. the *WiringViewer* agent detects a *Instant-FrequencyNCS* when an instant frequency of the spike produced by a *Neuron* agent it views is not good.

The nominal behaviour of a *Neuron* agent is to realize *integrate & fire model*. As a cooperative behaviour it detects *DepolarizationNCS* (the depolarization of a *Neuron* agent can be either lower than needed, higher than needed or good). Since “neurons fire together, wire together”, depolarization is crucial for *Neuron* agents. After this detection, it sends feedbacks to all its presynaptic agents. A *Neuron* agent, receiving either a *DepolarizationNCS* or *InstantFrequencyNCS* feedback, tries to increase its PSP or tries to find another *Neuron* agent to help it.

## 4. Related Work

In the literature, there are many models for the self-organization of neuronal networks. Schoenharl et al. [Schoenharl, 2005] developed a toolkit for computational neuroscientists to explore developmental changes in biological neural networks. However, details of the methodology used (e.g., how the initial random network is constructed) and of simulation parameters (e.g., how the threshold parameter for pruning is obtained) are not clear. Mano et al. [Mano and Glize, 2005] present an approach to self-organization in a dynamic neural network by assembling cooperative neuro-agents. However, their intent is not to explore synaptic connectivity. Maniadakis et al. [Maniadakis and Trahanias, 2009] addresses the development of brain-inspired models that will be embedded in robotic systems to support their cognitive abilities. How-

ever, this work focuses on brain slices rather than reflex pathways and aims to improve cognitive capabilities of robotic systems rather than exploring synaptic functional connectivity.

## 5. Conclusion & Future Work

Up until now, we have established and implemented a preliminary agent-based simulation model. The next step will be to enhance and to calibrate the proposed model. We will then compare *in silico* experiments with *in vitro* biological experiments. As a result of comparison we will either adjust our computational model or develop new/improved biological experiments to revise the biological model. This cycle will proceed until we get satisfactory results.

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